



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Medication shortages during the COVID-19 pandemic: Saving more than COVID lives



In the United States (US) alone, 3,302,194 cases and 135,171 deaths due to COVID-19 have been confirmed as of July 12th, 2020 [1]. To put this in perspective, from 2018–2019, the CDC estimated there were approximately 35,500,000 cases and 34,200 deaths due to influenza [2]. These statistics correspond to a case-fatality ratio (CFR), the number of deaths divided by the total number of confirmed cases, that is nearly 40 times that of influenza in the case of COVID-19 (CFR 0.1% and 4.0%, respectively). Over the course of the pandemic, hospital resources have become scarce. Shortages of PPE, healthcare personnel, and ventilators have been reported nationwide, now add medications to the list of shortages [3–5].

From 2015–2019, annual medication shortages have increased consistently from 5 to 31 (Fig. 1). However, over the span of only 6 months, 27 new shortages were announced in 2020 [6]. Medication shortages in 2020 have reached 87% that of the shortages reported in 2019 in half of the time. When considering the effect of the second wave of COVID-19 cases it is likely that medication shortages will continue to escalate.

One report of 44,672 confirmed cases of COVID-19 suggests 6168 (14%) patients suffer from severe hypoxic respiratory failure and 2087 (5%) required mechanical ventilation [7]. In the case of ventilation, patients often require varying amounts of sedation and/or analgesia

depending on their status. For example, fentanyl is a commonly used drug for analgesia, whereas propofol is used for sedation. In addition, midazolam can be infused if heavy sedation is required [8]. These medications are essential not patient comfort and to minimize the risk of self extubation. Yet, all 3 of these medications are currently in shortage (Table 1).

There is concern for additional patients presenting to emergency departments as states commit to reopening. One analysis suggests that the number of motor vehicle collisions (MVCs) decreased during the pandemic [9]. It is likely that the number of MVCs will return to baseline levels as additional states commit to reopening. The additional stress from trauma-related cases on the healthcare system in the midst of preexisting medication shortages could result in deaths that may have been preventable if ample medications were available.

Furthermore, medication shortages pose a threat to many more patients beyond those infected with COVID-19. For example, hydroxychloroquine and chloroquine are used for many autoimmune diseases such as rheumatoid arthritis. Although the shortages of these medications have recently resolved [6], other drugs such as dexamethasone used to treat both COVID-19 and many other diseases is depleting (Table 1).

With so much coverage on the pandemic, it is easy to forget about patients presenting with other common diseases. For example, heart disease remains the leading cause of death in the US and translates to 1 in every 4 deaths [10]. There is a shortage of medications used to treat those with cardiovascular disease, such as furosemide and labetalol injections (Table 1). Similarly, drugs used to prevent blood clots, such as heparin, are also currently in shortage (Table 1).

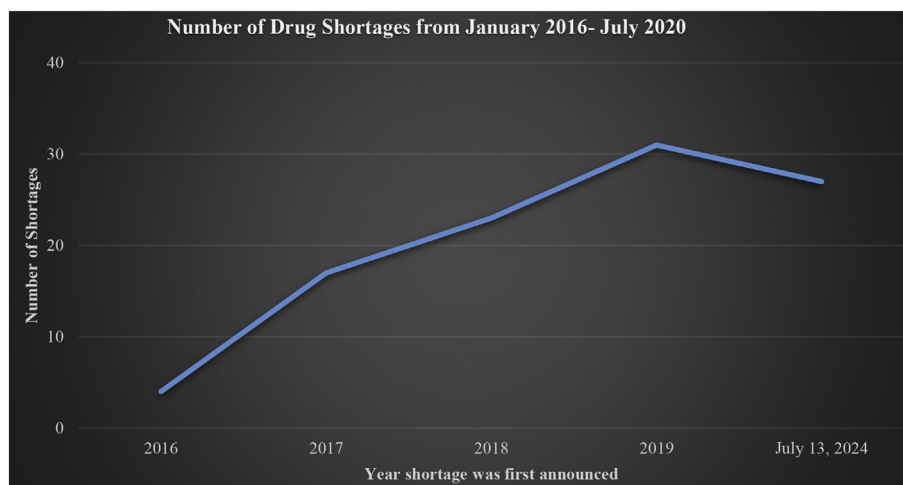


Fig. 1. Current Drug Shortages initially reported from January 2016 – July 12th, 2020. The number of drug shortages increased from 4 in 2016 to 17 in 2017. This represents a 325% increase in the number of drug shortages. Furthermore, the number of drug shortages increased to 23 in 2018, corresponding to a 35% increase. Moreover, there were 31 drug shortages initially reported in 2019, a 35% increase from 2018. Finally, 27 drug shortages were first reported from January 2020 – July 2020.

Table 1
Selected FDA Medication Shortages.

Selected medication shortages during the COVID-19 pandemic			
	Date first announced	Drug	Therapeutic category
2016	September 19th	Ketoprofen Capsules	Analgesia
2017	November 6th	Dopamine Hydrochloride Injection	Cardiovascular
	November 6th	Dobutamine Hydrochloride Injection	Cardiovascular, Renal
	November 14th	Heparin Sodium and Sodium Chloride 0.9% Injection	Hematology
2018	March 1st	Labetalol Hydrochloride Injection	Cardiovascular
	March 23rd	Ropivacaine Hydrochloride Injection	Anesthesia
	May 3rd	Lorazepam Injection, USP	Neurology
2019	September 12th	Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets	Psychiatry
	February 8th	Dexamethasone Sodium Phosphate Injection	Dermatology, Gastroenterology, Oncology, Ophthalmology, Pulmonary/Allergy, Rheumatology
	March 14th	Flurazepam Hydrochloride Capsules	Psychiatry
	April 2nd	Metoprolol Tartrate Injection, USP	Cardiovascular
	August 7th	Technetium Tc99m Succimer Injection (DMSA)	Medical Imaging
	February 26th	AVYCAZ (ceftazidime and avibactam) for Injection, 2 g/0.5 g	Anti-infective
2020	April 2nd	Hydrocortisone Tablets, USP	Endocrinology/Metabolism
	April 2nd	Midazolam Injection, USP	Anesthesia
	April 7th	Furosemide Injection, USP	Cardiovascular
	April 8th	Cisatracurium Besylate Injection	Anesthesia
	April 10th	Dexmedetomidine Injection	Anesthesia
	April 10th	Etomidate Injection	Anesthesia
	April 10th	Propofol Injectable Emulsion	Anesthesia
	April 14th	Azithromycin Tablets	Anti-infective
	April 22nd	Continuous Renal Replacement Therapy (CRRT) Solutions	Renal
	May 5th	Famotidine Injection	Gastroenterology
	May 6th	Vecuronium Bromide for Injection	Pulmonary/Allergy
	May 11th	Dimercaprol (Bal in Oil) Injection USP	Hematology
	May 21st	Amifostine Injection	Oncology
	July 10th	Doxycycline Hyclate Injection	Anti-infective
	N/A	Fentanyl Citrate (Sublimaze) Injection	Analgesia

Source: FDA Drug Shortages. U.S. Food & Drug Administration. <https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>. Accessed July 12th, 2020.

In addition, medication shortages will likely have an effect on cancer patients. Shortages of drugs used for medical imaging of cancer, such as Technetium, have the potential to compound the decrease in diagnoses due to the pandemic (Table 1). Furthermore, shortages of oncology medications that provide a protective effect from other chemotherapy agents, such as amifostine, may increase the risk for adverse events and worsen patient outcomes.

It is possible that as some medication shortages resolve, other shortages will arise and increase mortality. In 2017, over 1.7 million deaths were due to the top 5 causes of death: heart disease, cancer, unintentional injuries, chronic lower respiratory diseases, and stroke [11]. The medication shortages reported by the FDA thus far impact all 5 leading causes of death and could have a significant impact on the mortality rate. It is important for us to take proactive measures in order to minimize the negative effects on the nation.

In the same way manufactures of ventilators are increasing production, the manufacture of medications is a viable option. In addition, if companies such as Ford, Dyson and Tesla were able to create ventilators, large pharmaceutical companies could focus on producing drugs in shortage [5]. In addition to increased manufacturing, domestic production of the active ingredient of essential drugs can aid in the shortage, as some drugs are scarce for this reason. The consequences may be dire for those whose life relies on these medications. Although it is still a long road back to normalcy, when the pandemic is over, we may never know if our efforts reached the point of overkill, however, it will be very obvious to us if we did not do enough.

References

- [1] COVID-19 map. Johns Hopkins Coronavirus Resource Center; 2020 <https://coronavirus.jhu.edu/map.html> Published January 22, 2020. Accessed July 12th, 2020.
- [2] Estimated influenza illnesses, medical visits, hospitalizations, and deaths in the United States – 2018–2019 influenza season. Centers for Disease Control and Prevention; 2020 https://www.cdc.gov/flu/about/burden/2018-2019.html#anchor_1571233384487 Accessed July 12th, 2020.
- [3] Strategies to mitigate healthcare personnel staffing shortages. Centers for Disease Control and Prevention; 2020 <https://www.cdc.gov/coronavirus/2019-ncov/hcp/mitigating-staff-shortages.html> Reviewed April 30th, 2020. Accessed July 12th, 2020.
- [4] Strategies to optimize the supply of PPE and equipment. Centers for Disease Control and Prevention; 2020 <https://www.cdc.gov/coronavirus/2019-ncov/hcp/ppe-strategy/index.html> Reviewed July 10th, 2020. Accessed July 12th, 2020.
- [5] Ventilator stockpiling and availability in the US. Johns Hopkins Center for Health Security; 2020 <https://www.centerforhealthsecurity.org/resources/COVID-19/COVID-19-fact-sheets/200214-VentilatorAvailability-factsheet.pdf> Published July 1st, 2020. Accessed July 12th, 2020.
- [6] FDA drug shortages. U.S. Food & Drug Administration; 2020 <https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm> Accessed July 12, 2020.
- [7] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239–42. <https://doi.org/10.1001/jama.2020.2648>.
- [8] Vizient. COVID-19 Impact on drugs essential for ventilator use. Published April 7th, 2020. https://newsroom.vizientinc.com/sites/vha.newshq.businesswire.com/files/doc_library/file/COVID-19_impact_upon_ventilator_products_UPDATED2.1_040720.pdf. Accessed July 12th, 2020, 2020.
- [9] Sutherland M, McKenney M, Elkbuli A. Vehicle related injury patterns during the COVID-19 pandemic: what has changed? Am J Emerg Med. 2020;38(9):1710–4. <https://doi.org/10.1016/j.ajem.2020.06.006> Online ahead of print. PMID: 32721782.

- [10] Heart disease facts. Centers for Disease Control and Prevention; 2020 <https://www.cdc.gov/heartdisease/facts.htm> Reviewed June 22nd, 2020. Accessed July 12th, 2020.
- [11] Leading causes of death. Centers for Disease Control and Prevention; 2020 <https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm> Reviewed March 17th, 2017. Accessed July 12th, 2020.

Brendon Sen-Crowe

*Department of Surgery, Division of Trauma and Surgical Critical Care,
Kendall Regional Medical Center, Miami, FL, USA*

Mark McKenney MD, MBA

*Department of Surgery, Division of Trauma and Surgical Critical Care,
Kendall Regional Medical Center, Miami, FL, USA
University of South Florida, Tampa, FL, USA*

Adel Elkbuli MD, MPH

*Department of Surgery, Division of Trauma and Surgical Critical Care,
Kendall Regional Medical Center, Miami, FL, USA*

Corresponding author at: 11750 Bird Road, Miami, FL 33175, USA.

E-mail address: Adel.Elkbuli@hcahealthcare.com

15 July 2020